# Using Portfolio Analysis on Druggable Genome Common Fund Program

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## Introduction

The “druggable genome” is the set of genes encoding proteins known or predicted to be regulated by small molecule compounds, or “drugs”. The NIH launched an FY14 Common Fund (CF) program entitled “Illuminating the Druggable Genome” (IDG) to encourage the exploration of understudied proteins in four classes of drug targets: G-protein-coupled receptors (GPCRs), nuclear receptors (NR), ion channels, and protein kinases. This program is intended to help address the current shortage of new therapeutic drugs.

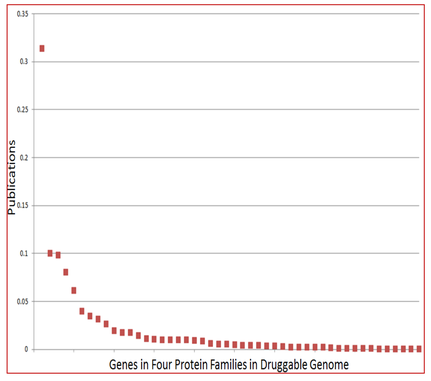
Our portfolio analysis helped the IDG CF Working Group select the “understudied” proteins on which to focus in the FOA. Considering the complexity and scale size of portfolio analyses of 1242 genes in the druggable genome, here we used the nuclear receptor family, consisting of 48 NRs, as a case study to illustrate how portfolio analysis helped the IDG program. This analysis was also an opportunity to explore the use of various data resources and approaches in identifying gaps in druggable genome research.

## Methods

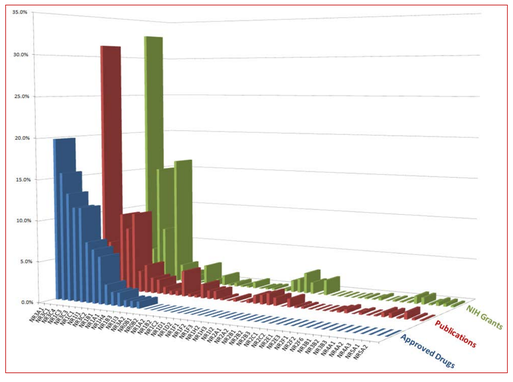
- Published research papers of 48 nuclear receptors in PubMed from 1940 through May 2014.
- Publications supported by NIH grants, identified by using the SPIRES database.
- NIH awarded grants for all nuclear receptors from FY03 to FY13, identified by searching gene names and aliases in all titles, abstracts, and specific aims.
- Drugs and indications (approved, in clinical development) for NRs were analyzed by using FDA drug database and target drug database.

## Results

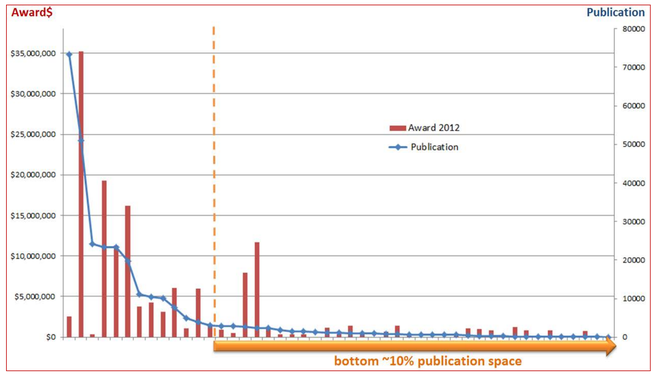
### Overall Publications



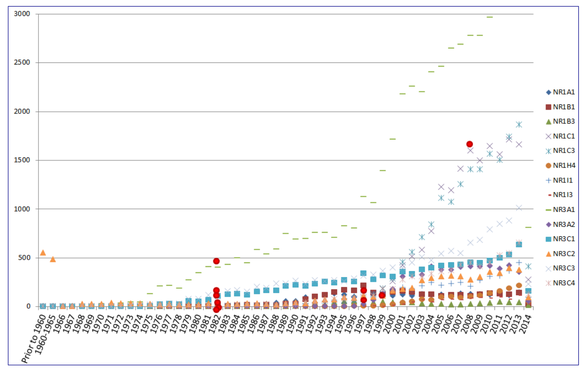

### Publications, Grants, and Approved Drugs for NRs



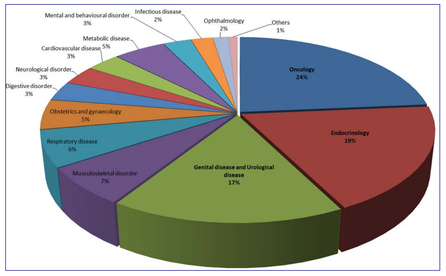

### “Understudied” Nuclear Receptors



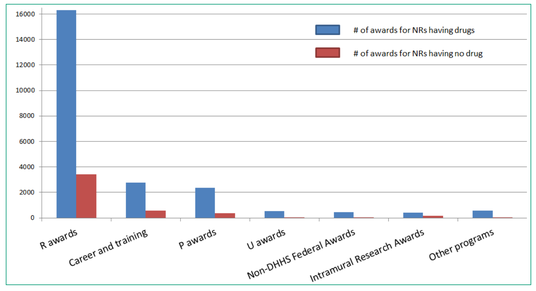

### Correlation of Drug approval with Publications



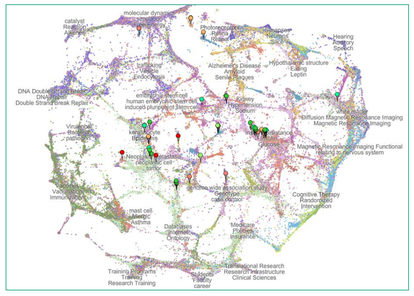

### Indications of Drugs for NRs




### NIH Awards (FY03 - FY13) for NRs by Funding Mechanisms




### Scientific Topics of Funded *NR1C2* Programs



## Conclusions

- Overall publication data demonstrate the power law effect across all protein families.
- Portfolio analysis helped the IDG CF program define the “understudied” proteins in the FOA, where they account for only the bottom 10% of the overall publication space.
- NIH contributed ~21% of published findings in nuclear receptor research.
- Fourteen nuclear receptors have ~ 120 therapeutic drugs approved, predominantly for treatment of Cancer and Endocrinology disease.
- Approximately half of the NIH awards were R01s.
- Time to launch a drug doesn’t always correlate with an increase of publications.
- Nuclear receptor *NR1C2* is one of the most promising druggable targets for NIH future investment, as it has been under clinical development for metabolic syndrome and skin disease.

**Acknowledgement: IDG CF Working Group**